REMARKS

Claims 1 and 3-12 are pending. Claims 13-16 have been withdrawn from consideration. Claim 17 has been newly added. Support for claim 17 is found at paragraphs [**0053**] and [**0063**] through [**0065**]. Claim 2 has been cancelled. Claims 1-12 have been rejected. Claims 2-12 have been objected to. Claim 3 has been amended to make it dependent on claim 1. Claim 1 has been amended. No new matter has been added by the amendments.

Examiner Interview

The undersigned thanks the Examiner for the telephone interview on February 20, 2008. During the interview, the proposed cancellation of claim 2 and amendment to claim 1 deleting reference to mass spectrometry was discussed. The Examiner agreed that the cancellation of claim 2 and amendment to claim 1 would overcome each of the objections and rejections in the outstanding Office Action. Applicant has, therefore, cancelled claim 2 and has deleted the mass spectrometry limitation recited in claim 1.

The Examiner further indicated that he never searched any methods of DNA sequencing except mass spectrometry. He would, therefore, be conducting a further search including Sanger and/or pyrosequencing in the context of the invention. Applicant has herein deleted the Sanger sequencing limitation of claim 1. Applicant is further concurrently submitting a supplemental IDS with 1 reference relating to pyrosequencing technologies.

Objections under 37 C.F.R. § 1.75(c)

Claims 2-12 have been objected to under 37 C.F.R. § 1.75(c) for failing to further limit the subject matter of the previous claim. Claim 2 has been cancelled, therefore the objection is moot.

Rejections under 35 U.S.C. § 112

Claims 2-12 have been rejected under 35 U.S.C. § 112, 2nd paragraph, for indefiniteness since the limitation "the sequencing reaction" in lines 1-2 of claim 2 has insufficient antecedent basis. Claim 2 has been cancelled, therefore the rejection of claims 2-12 is moot.

Rejections under 35 U.S.C. § 102

Claims 2-5 have been rejected under 35 U.S.C. § 102(b) as anticipated by WO 96/06187 to Tully et al.

Tully discloses a method for single nucleotide polymorphism analysis using nucleotide primers complementary to a characterized base sequence extended by a single dye-labeled di-deoxynucleoside triphosphate (ddNTP). Thus, "...chain extension by the chain extending enzyme terminates after the addition of only one base which is complementary to the base being determined." See pages 2 and 3 of Tully. It is the position of the Examiner that Tully teaches the invention as presently claimed. This is not the case.

Applicant's Response

The method of the present invention uses pyrosequencing, as recited in claim 1 and exemplified in Example 2 of the application. This method of sequencing explicitly requires at a minimum a plurality of base extensions for adequate analysis. *See* Ronaghi et al., "A Sequencing Method Based On Real-time Pyrophosphate" Science 281(5375):363-365 (1998). Therefore, the method of Tully in which chain extension must terminate after only one base cannot anticipate, either expressly or inherently, claims 2-5 of the present invention.

The Examiner considered the above arguments in the Office Action Response dated October 7, 2008 finding them unpersuasive because "...claim 2 effectively broadens the claimed method such that it encompasses the sequencing methods according to Tully..." Claim 2 has been cancelled. Therefore, the methods disclosed in Tully

cannot anticipate, either expressly or inherently, claims 3-5. The removal of this rejection is requested.

Claims 2-5 have been rejected under 35 U.S.C. § 102(b) as anticipated by Ye et al., "Fluorescent Microsphere-based Readout Technology For Multiplexed Human Single Nucleotide Polymorphism Analysis and Bacterial Identification" Human Mutation 17:305-316 (2001). Ye discloses a method for single nucleotide polymorphism analysis involving hybridizing biotin-labeled single nucleotide primers to target base sequences, hybridizing the labeled target base sequences to beads and analyzing by flow cytometry. It is the position of the Examiner that Ye teaches the invention as presently claimed. This is not the case.

Applicant's response

Nowhere does Ye teach or suggest "...extending the hybridized primer or primers using pyrosequencing", as recited in claim 1.

The Examiner considered the above arguments in the Office Action Response dated October 7, 2008 finding them unpersuasive because "...claim 2 effectively broadens the claimed method such that it encompasses the sequencing methods according to Ye..." Claim 2 has been cancelled. Therefore, the methods disclosed in Ye cannot anticipate, either expressly or inherently, claims 3-5. The removal of this rejection is requested.

Claim 1 has been rejected under 35 U.S.C. § 102(b) as anticipated by Bray et al., "High-Throughput Multiplex SNP Genotyping With MALDI-TOF Mass Spectrometry: Practice, Problems and Promise" Human Mutation 17:296-304 (2001). Bray discloses multiplex single nucleotide polymorphism genotyping using mini-sequencing reactions followed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. It is the position of the Examiner that Bray teaches the invention as presently claimed. This is not the case.

Applicant's response

Nowhere does Bray teach or suggest, either expressly or inherently, the use of pyrosequencing as a DNA sequencing method, as recited in claim 1 of the present

invention. Bray, rather, discloses the use of mini-sequencing reactions "...using oligonucleotide primers that anneal immediately 5' of each polymorphic site, dideoxynucleotides and a thermostable polymerase used to extend the PCR product by a single base pair..." Page 298, second full paragraph. Pyroseqeuncing, in contrast, explicitly requires at a minimum a plurality of base extensions for adequate analysis. Removal of the rejection is requested.

Rejections under 35 U.S.C. § 103

Claims 6-12 have been rejected under 35 U.S.C. § 103(a) for obviousness over Tully in view of Rady.

Rady discloses a method of detecting human papillomavirus (HPV) types by sequencing of target HPV-DNA fragments using consensus primers and type-specific HPV primers in separate individual sequencing reactions.

As discussed above, Tully does not anticipate independent claim 1 of the present invention. The Examiner has made no showing that Rady remedies the deficiencies of Tully with respect to claim 1, either expressly or inherently. Therefore, claims 6-12, which are dependent on claim 1, are likewise not obvious over Tully in view of Rady.

For the above reasons, the rejection of claims 6-12 should be withdrawn.

Claims 6-12 have been rejected under U.S.C. § 103(a) for obviousness over Ye in view of Rady.

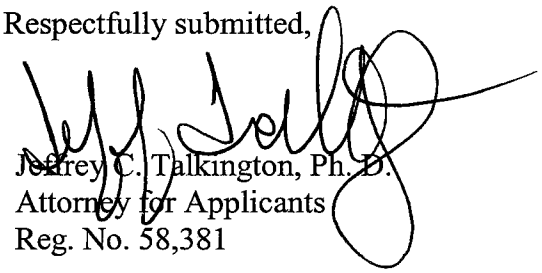
As discussed above, Ye does not anticipate independent claim 1 of the present invention. The Examiner has made no showing that Rady remedies the deficiencies of Ye with respect to claim 1, either expressly or inherently. Therefore, claims 6-12, which are dependent on claim 1, are likewise not obvious over Ye in view of Rady.

For the above reasons, the rejection of claims 6-12 should be withdrawn.

Conclusion

All claims are in a condition for allowance. The issuance of a Notice of Allowability, therefore, is respectfully requested. Should the Examiner have any questions or concerns, the Examiner is invited to call the undersigned attorney of record.

Respectfully submitted,



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